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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,574	11/07/2001	Fabienne MacKay	08201.0024-01000	9312

7590 07/02/2003

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	12

DATE MAILED: 07/02/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,574	MACKAY ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- Th MAILING DATE of this communication appears on th cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *1-51,54-56 and 58-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52,53 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-62 are pending.

2. Applicant's election with traverse of Group LVI, claims 52-53 and 57 drawn to a method for treating or reducing the advancement, severity or effects of Sjogren's syndrome in a patient comprising administering BAFF receptor, BAFF-R filed on 4/22/03, is acknowledged.

Applicant's traversal is on the grounds that no serious burden on the Examiner is shown that is no different fields of search have been shown. Further, the examiner does not explain what structureal differences in the "products" or "steps" would necessitate a field of search where no pertinent art to the other subject exist. This is not found persuasive because the specific TACI, BCMA, and BAFFR are recognized divergent subject matter. Therefore the methods of treating or reducing the advancement, severity or effects of Sjogren's syndrome comprising administering TACI, BCMA, and BAFFR are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-51, 54-56 and 58-62 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 52-53 and 57 are under examination as they read on a method for treating or reducing the advancement, severity or effects of Sjogren's syndrome in a patient comprising administering BAFF receptor, BAFF-R.

5. There is a discrepancy between the Declaration and the Specification on page 1, line 5, regarding the filing date of U.S.S.N 60/143,228. The Declaration indicates that U.S.S.N 60/143,228 was filed July 9, 1999, while the specification discloses that U.S.S.N 60/143,228 was filed July 9, 2001. Examiner notes that U.S.S.N 60/143,228 was filed July 9, 1999. Correction is required.

6. The disclosure is objected to because of the following informalities: page 9, lines 1-2, discloses that SEQ ID NO:1 and 2 are human and mouse BAFF, respectively, while Figure 1A depicts to SEQ ID NO:1&2 as hMARCH and mMARCH respectively. Similar issues are depicted on figures 1B-1C and Figure 2B. Page 11, lines 3-7, disclose the use of BAFF ligand, however, Figure 6, depicts the use of Kay Ligand (kayl). Appropriate correction is required.

7. The specification is objected to under 37 CFR 1.821(d) for failing to provide a sequence identifier for each individual sequence. Page 32, line 15 has described three motifs in BAFF, APRIL and Tweak wherein each must have a sequence identifier. Correction is required.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 52-53 and 57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for a method for treating or reducing the adancement, severity or effects of Sjogren's syndrome in a patient comprising the step of administering a pharmaceutical composition comprising a therapeutically effective amount of a BAFF blocking agent and a pharmaceutically acceptable carrier in claim 1, wherein the BAFF blocking agent is a soluble BAFF receptor molecule in claim 53, wherein the BAFF receptor is BAFF R in claim 57. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is insufficient guidance and direction as to make and use BAFF blocking agents, any soluble BAFF receptor molecule or any BAFF-R. Furthermore, the specification fails to provide empirical data to show that method would work in vivo. Finally, the specification fails to provide structure for the BAFF-R.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies such "BAFF blocking agents" other than human BAFF-R (GenBank accession number AF373846) and mouse BAFF-R (GenBank accession number AF373847) improperly incorporated by reference (page 17, lines 7-8). While "BAFF blocking agent" may have some notion of the activity of the "agents", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use such "agents", commensurate in scope with the claimed invention. It has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Applicant has not enabled structurally related and unrelated compounds comprising "any BAFF blocking agent" (page 16, last paragraph of the specification) which would be expected to have greater differences in their

biological activities. There is insufficient direction or objective evidence as to how to make and to how to use any agent which diminish BAFF ligand binding to BAFF-R for the number of possibilities associated with the myriad of direct and indirect effects associated with various BAFF receptors and hence pathways or molecules and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Because of this lack of guidance, the extended experimentation that would be required to determine which modifications would be acceptable to retain occluding structural and functional activity, and the fact that the relationship between the sequence of a protein/peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g. see Ngo et al.; in The Protein Folding Problem and Tertiary Structure Prediction,1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.), it would require an undue amount of experimentation for one of skill in the art to arrive at the other BAFF blocking agent encompassed by the claimed invention.

The incorporation of essential material in the specification by reference to Thompson et al (Science 293:2108, 2001) (page 17, lines 6-7) is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

The attempt to incorporate subject matter into this application by reference to Thompson et al (Science 293:2108, 2001) is improper because an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, see MPEP 608.01(p),. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Further, applicant is required to incorporate this essential subject matter from Thompson et al (Science 293:2108, 2001, see page 17, lines 7-8 of the specification) for BAFF R sequence in the specification and claims. Furthermore, Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825).

Further, at issue is whether or not the claimed method would function to treat or reduce the advancement, severity or effects of Sjogren's syndrome. The nature of the invention is such that it would require the administration of soluble BAFF-R receptor that would treat/reduce Sjogren's syndrom. The specification (pages46, under example 7) discloses BAFF transgenic mice

develop a Sjogren-like syndrome with age. The specification further discloses that mice with severe lesions in their submasxillary glands did not secrete anti-Ro/SSA and/or anti-LA/SSB autoantiboides, which are often associated with human SS (page 48, lines 1-5). The specification does not provide empirical data to show the efficacy of active immunization with soluble BAFF-R on SS, wherein the soluble BAFF-R would function to treat/reduce severity of SS. It is not clear that the skilled artisan could predict the efficacy of the soluble BAFF-R on SS, encompassed by the claims. Dang et al (J Immunol. 155(6):3205-3212, 1995) teach that Mice bearing the TGF-beta 1 null mutation (-/-) develop lymphoid infiltrates in the heart, lungs, salivary glands, and other organs similar to those seen in the pseudolymphoma of Sjogren's Syndrome. Dang et al further teach that the sera from -/- mice and found elevated Ab levels to dsDNA, ssDNA, and Sm ribonucleoprotein. No Abs to SSA/Ro or SSB/La and no IgM rheumatoid factor were found. Dang et al teach that treating the TGF-β -/- mice with dexamethasone or TGF-beta 1 failed to suppress autoantibody production (Abstract and page 3208, 2nd col., 2nd ¶, in particular). Therefore, it is unpredictable whether treatment of SS with soluble BAFF-R would reach a therapeutic end point. It is not clear that the skilled artisan could predict the efficacy of the soluble BAFF-R on Sjogren's syndrome.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. Claims 52-53 and 57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is not in possession of a method for treating or reducing the adancement, severity or effects of Sjogren's syndrome in a patient comprising the step of administering a pharmaceutical composition comprising a therapeutically effective amount of a BAFF blocking agent and a pharmaceutically acceptable carrier in claim 1, wherein the BAFF blocking agent is selected from the group consisting of a soluble BAFF receptor molecule in claim 53, wherein the BAFF receptor is BAFF-R in claim 57.

Applicant has disclosed only amino acid of human and mouse BAFF-R (GenBank accession No. AF373846 and AF373847, respectively); therefore, the skilled artisan cannot envision all the contemplated BAFF blocking agent possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be

satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Patent Examiner
Technology Center 1600
June 30, 2003

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